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(HEALTH AFFAIRS)**

**SUBJECT: Management of Traumatic Brain Injury in Tactical Combat Casualty Care
2012-04**

EXECUTIVE SUMMARY

Of 355,425 diagnoses of traumatic brain injury (TBI) between 2000 and 2011, 45,131 were moderate, severe or penetrating.¹ The Department of Defense (DoD) has made significant advancements in expanding guidance regarding the treatment of Service members with mild TBI (mTBI), but limited guidance exists for the treatment of casualties with severe TBI, especially on the battlefield. The Tactical Combat Casualty Care (TCCC) Guidelines are currently the standard used for training medics and many other deploying medical providers. As such, the Defense Health Board (DHB) recommends amending the TCCC Guidelines to include guidance for the treatment of casualties with suspected moderate/severe TBI, simply defined as penetrating brain injury or head injury with altered level of consciousness. This report provides an overview of the issue and the recommended additions to the TCCC Guidelines, as provided by the Committee on Tactical Combat Casualty Care (CoTCCC), and subsequently approved by the Trauma and Injury Subcommittee and DHB.

OVERVIEW OF THE ISSUE

In October 2007, DoD established a formal definition of TBI as “a traumatically induced structural injury and/or physiologic disruption of brain function as a result of (the) external force.”² Current DoD initiatives include detailed clinical practice guidelines (CPGs) and increased provider training. The remaining gaps are the treatment of casualties with moderate to severe TBI at the point of injury and during transport. During this time, moderate brain injury can evolve into severe brain injury and casualties are at risk of secondary brain injury, which occurs most often in casualties with moderate/severe TBI.³ To prevent secondary brain injury, which worsens outcome and increases mortality from moderate/severe TBI, treatment of suspected moderate/severe TBI should begin as soon as possible.⁴

TACTICAL COMBAT CASUALTY CARE GUIDELINES

The TCCC Guidelines are a set of trauma care guidelines customized for use in the prehospital combat setting. The Guidelines identify three stages of care: (1) Care under Fire; (2) Tactical Field Care; and (3) Tactical Evacuation (TACEVAC) Care. TCCC is currently used in training for medics by all Services in DoD and by many U.S. coalition partners.^{5, 6} The CoTCCC, a work group of the DHB Trauma and Injury Subcommittee, performs a quarterly review of current evidence demonstrating the successes and shortcomings of the TCCC Guidelines, and considers proposed updates and revisions.^{5, 6} The current TCCC Guidelines provide limited guidance for

the management of casualties with moderate/severe TBI and lack a dedicated section for this issue.

METHODOLOGY

The CoTCCC recently reviewed the TCCC Guidelines to ensure they reflect the current best practice for the prehospital treatment of casualties with moderate/severe TBI. Overall, the available evidence base regarding prehospital and combat TBI management best practices is weak, with published studies often citing low quality or primarily anecdotal evidence. The Brain Trauma Foundation (BTF) rigorously evaluated the available evidence and developed guidelines based on the best available evidence. These guidelines are available in the *Guidelines for Prehospital Management of Traumatic Brain Injury, 2nd edition*, released in 2007 and the *Guidelines for Field Management of Combat-Related Head Trauma*, released in 2005.* The Joint Theater Trauma System (JTTS) CPG for the Management of Patients with Severe Head Trauma provides additional guidance. The CoTCCC reviewed these guidelines in addition to select medical literature that addresses prehospital management of patients with severe head trauma. Trauma and Injury Subcommittee and CoTCCC member Dr. Mel Otten led the review. Based on his assessment, he proposed changes to the TCCC Guidelines to the CoTCCC on November 14, 2012. Additional input was garnered from Dr. Donald Marion (Defense Centers of Excellence for Psychological Health and TBI (DCoE)), CAPT Paul Hammer (Director of DCoE), Dr. George ‘Peach’ Taylor (Deputy Assistant Secretary of Defense (Force Health Protection and Readiness)), Dr. Alan Frankfurt (anesthesiologist), and CAPT David Tarantino, (Headquarters Marine Corps). Where possible, this report provides the quality of evidence and strength of recommendations as assessed by BTF, as well as additional evidence published since the release of the BTF guidelines.

At the February 7, 2012 CoTCCC meeting, Dr. Otten presented proposed revisions to the guidelines as well as feedback from TBI subject matter experts. The members deliberated and amended the proposed changes on February 7-8, 2012. The CoTCCC agreed by unanimous vote on February 8, 2012 to forward its recommendations to the Trauma and Injury Subcommittee for review. The Trauma and Injury Subcommittee subsequently passed the recommended changes later that day. On June 25, 2012, Dr. Otten presented the proposed recommendation to the DHB, after which the Board discussed the recommended changes and voted to provide this recommendation report to the Assistant Secretary of Defense (Health Affairs). An overview of the Board’s discussion is provided later in this report.

EVIDENCE

Prevention of secondary brain injury involves aggressive treatment to prevent hypoxia and hypotension. The primary elements of prehospital care for casualties with severe TBI are to avoid hypotension (systolic blood pressure (SBP) < 90 mmHg) and hypoxemia (oxygen saturation < 90%).^{3, 4, 7} These recommendations are in the current TCCC Guidelines and have been the cornerstone of the TCCC Curriculum for casualties with severe TBI since 2003. These and additional considerations for casualties with severe or penetrating head injury which are recommended for inclusion in the TCCC Guidelines are reviewed in further detail below.

* Of note, the committee that developed the Guidelines included two CoTCCC members.

Hypotension and Hypoxemia

Hypoxemia and hypotension may worsen outcomes for casualties with moderate/severe TBI. In its *Guidelines for the Prehospital Management of Severe Traumatic Brain Injury (Second Edition)*, BTF recommends that patients with moderate/severe TBI be monitored for hypoxemia via pulse oximetry (defined as less than 90 percent arterial hemoglobin oxygen saturation) and hypotension (defined as less than 90 mmHg SBP) using the most accurate means available.³ These recommendations are consistent BTF's *Guidelines for Field Management of Combat-Related Head Trauma*.⁷ BTF categorized the strength of these recommendations as weak and the quality of evidence as low (primarily from Class III studies and indirect evidence).³ However, since the guidelines were published in 2007, additional published articles, as well as the JTTS CPG for Management of Patients with Severe Head Trauma, have supported these recommendations (note: the JTTS CPG recommends that blood oxygen saturation be maintained at greater than 93 percent).^{8, 9, 10, 11} Medics do not currently carry oxygen in their combat medical sets, but oxygen may be available at Casualty Collection Points established for larger military operations. As such, the CoTCCC recommends adding a note to the Tactical Field Care section stating that medics should use oxygen if available.

Fluid Resuscitation

The TCCC Guidelines currently indicate a modified fluid resuscitation regimen for casualties suffering from both shock and TBI. In these casualties, unconsciousness or altered mental status may be caused by either head injury or hypovolemic shock. Both BTF guidelines recommend hypertonic saline resuscitation, as it may help reduce cerebral edema and intracranial pressure (ICP) and correct hypotension (NOTE: the evidence quality is low, from Class II studies with contradictory findings, and the recommendation strength is classified as weak).^{3, 7} BTF's *Guidelines for Field Management of Combat-Related Head Trauma* indicate that fluids should not be instituted in the presence of a strong radial pulse (indicating that the patient is likely not in hemorrhagic shock).⁷ Since these guidelines were published, Strandvik conducted a systematic review and concluded that hypertonic saline solutions are effective in restoring blood pressure in patients with hemorrhagic shock and in reducing ICP.¹² Another systematic review by Meyer et. al. concludes that hypertonic saline improves ICP.¹³ Bulger et. al. conducted a large randomized, blinded, placebo-controlled trial of the early administration of hypertonic fluids on patients with presumed severe TBI, without evidence of hypovolemic shock; study authors found no benefit in giving hypertonic fluids over normal saline.¹⁴ Rockswold et. al. conducted a prospective study in a controlled hospital environment on patients with severe TBI and found that hypertonic saline decreased ICP and improved cerebral perfusion pressure (CPP) and brain tissue oxygen tension.¹⁴ The evidence is consistent with the current TCCC Guidelines; additionally, the CoTCCC recommends including the use of hypertonic saline for resuscitation in patients with TBI in the proposed new section of the TCCC Guidelines dedicated to TBI management.

Opioids

Adverse effects of opioid analgesic medications include respiratory depression and hypotension,¹⁶ which may worsen outcomes following TBI.^{3, 17} Because of this risk, there has been a long-standing warning in the TCCC Curriculum and the *Pre-Hospital Trauma Life Support Manual (Military Edition)* regarding the use of these agents in casualties with pulmonary dysfunction, shock, or altered state of consciousness.⁵ Upon reviewing the current

TCCC Guidelines, CoTCCC members agreed that such a warning should also be included in the TCCC Guidelines.

Hypothermia

Two retrospective studies of trauma patients admitted to U.S. hospitals have demonstrated that nontherapeutic hypothermia has a statistically significant negative impact on mortality in patients with TBI.^{18, 19} Because the TCCC Guidelines address hypothermia prevention in detail, no additions are recommended regarding this factor.

Head Elevation

Although neither of the BTF Guidelines recommend head elevation, low-level evidence suggesting that head elevation may help decrease ICP (based on studies conducted in a hospital environment) has warranted its inclusion in the JTTS CPG.¹⁰ The evidence for this recommendation primarily comes from two small randomized controlled trials and case series studies. Meyer et. al. conducted a systematic review of literature found in several databases between 1980 and 2008, in which they categorized the evidence that 30 degree head elevation decreases elevated ICP and increases CPP as level II (findings supported by a single randomized controlled trial of at least fair quality).²⁰ Since negative effects of the positioning are unlikely, the CoTCCC recommends that elevation of the casualty's head by 30 degrees be included in the TCCC Guidelines for casualties with suspected severe TBI.

Hyperventilation

Routine hyperventilation of casualties with TBI in the absence of impending cerebral herniation has been noted by multiple authors to be either of no benefit or to be harmful (it may decrease cerebral blood flow). It is not recommended by BTF and a Cochrane Review concluded that there is not enough evidence to determine whether it improves outcomes for people with TBI.^{3, 7, 8, 11, 21} As such, the CoTCCC supports BTF's recommendation that hyperventilation should be avoided unless there is evidence of impending cerebral herniation.³ Because hyperventilation causes cerebral vasoconstriction, medics may use it as a temporizing measure to reduce ICP in the event there is evidence of cerebral herniation. BTF's recommendations suggest that asymmetric, unilateral or bilateral dilated pupils may indicate cerebral herniation.^{3, 7} However, BTF notes that the strength of this recommendation is weak, lacking adequate sensitivity and specificity to predict the injury pattern or clinical course, citing low quality evidence from Class III studies and indirect evidence.^{3, 8, †} Periods of hyperventilation should be as brief as possible. BTF indicates that the strength of this recommendation is weak, and the quality of evidence is low (primarily from Class III studies).^{3, 7, 8} Capnography should be used whenever available to maintain the end-tidal CO₂ between 30 and 35.^{3, 8} A respiratory rate of 20 (breaths per minute) may be used in the absence of capnography.⁷ The highest fraction of inspired oxygen (FiO₂) possible should be used for hyperventilation in casualties with signs of impending cerebral herniation. Hyperoxia causes cerebral vasoconstriction independently of the effects of

[†]BTF recommends in both its prehospital and combat-trauma guidelines that the Glasgow Coma Scale (GCS) be assessed in addition to pupil examination; however, CoTCCC members felt it would be too challenging for medics to remember, especially since a study of Emergency Medicine Technicians-Basic found that few could correctly calculate the GCS without a reference card or immediately following training.⁷ No studies have been published validating the use of the GCS in the military prehospital setting. Current TCCC documentation on DA Form 7656 uses AVPU (Alert, arousable to Voice, Pain or Unarousable), a standard prehospital neurological assessment scheme.

hypocapnia.^{22, 23} Hyperoxia has been shown to increase cerebral tissue oxygenation²³ and to improve neurochemical markers suggesting an increase in cerebral oxidative metabolism in casualties with severe head injury.^{24, 25, 26, 27}

Antibiotics

The *Guidelines for the Prevention of Infections Associated with Combat-Related Injuries, 2011 Update* indicate that various guidelines and animal studies support the premise that early administration of antimicrobials can delay the onset of infection and are beneficial. These guidelines also state that retrospective reviews and expert opinion support post-injury antimicrobials for the prevention of infection in casualties with penetrating brain injury.²⁸ Further, the *Guidelines for the Management of Penetrating Brain Injury* (2001) note that “If Class I and II evidence supports the use of antibiotics in a clean wound made under controlled conditions, the use of antibiotics in a grossly contaminated penetrating wound appears justified.”²⁹ Based on these guidelines, the authors of the *Guidelines for Field Management of Combat-Related Head Trauma* offer the same recommendation. CoTCCC members agreed that antibiotics are not necessary for closed head injury, but should be given to individuals with penetrating head injury.¹⁰

DELIBERATIONS

As noted above, Dr. Otten presented the recommended changes to the Board at its meeting on June 25, 2012. The DHB members discussed the recommended changes to the Guidelines at length and strongly concurred with the findings and recommendations of the Trauma and Injury Subcommittee. They also agreed that the GCS is likely not practical in a theater setting and that AVPU would be sufficient despite previous recommendations from the BTF that GCS should be used. Members noted that the lack of prehospital data in theater (a preliminary report from the U.S. Army Institute of Surgical Research suggest that information is collected for only 15 percent of casualties) is an ongoing problem that should be addressed to increase the prehospital care evidence base, including for TBI management in the field.

CONCLUSION

The DHB concludes that the changes to the TCCC Guidelines proposed by the CoTCCC and approved by the Trauma and Injury Subcommittee reflect the best available evidence and most important aspects of prehospital care for casualties with moderate/severe TBI based on the consensus-derived opinion of CoTCCC and Trauma and Injury Subcommittee members. Because the DHB notes a paucity of robust evidence-based research regarding prehospital (and battlefield) treatment of suspected severe TBI, the Board further recommends that the DoD make priorities prehospital data collection and additional research regarding prehospital management of moderate/severe TBI.

RECOMMENDATIONS

The Board recommends that DoD incorporate the following changes regarding the management of moderate/severe TBI to the TCCC Guidelines (additions are underlined below). These

additions will help combat medics, corpsmen, and Pararescuemen recognize and treat impending cerebral herniation in TBI casualties on the battlefield and during evacuation.

Tactical Field Care

3. Breathing

- a. In a casualty with progressive respiratory distress and known or suspected torso trauma, consider a tension pneumothorax and decompress the chest on the side of the injury with a 14-gauge, 3.25 inch needle/catheter unit inserted in the second intercostal space at the midclavicular line. Ensure that the needle entry into the chest is not medial to the nipple line and is not directed towards the heart.
- b. All open and/or sucking chest wounds should be treated by immediately applying an occlusive material to cover the defect and securing it in place. Monitor the casualty for the potential development of a subsequent tension pneumothorax.
- c. Casualties with moderate/severe TBI should be given supplemental oxygen when available to maintain an oxygen saturation > 90%.

10. Monitoring

Pulse oximetry should be available as an adjunct to clinical monitoring. All individuals with moderate/severe TBI should be monitored with pulse oximetry. Readings may be misleading in the settings of shock or marked hypothermia.

13. Provide analgesia as necessary.

a. Able to fight:

These medications should be carried by the combatant and self-administered as soon as possible after the wound is sustained.

- Mobic, 15 mg PO once a day
- Tylenol, 650-mg bilayer caplet, 2 PO every 8 hours

b. Unable to fight:

Note: Have naloxone readily available whenever administering opiates.

- Does not otherwise require IV/IO access
 - Oral transmucosal fentanyl citrate (OTFC), 800 ug transbuccally
 - Recommend taping lozenge-on-a-stick to casualty's finger as an added safety measure
 - Reassess in 15 minutes.
 - Add second lozenge, in other cheek, as necessary to control severe pain.
 - Monitor for respiratory depression.
- IV or IO access obtained:
 - Morphine sulfate, 5 mg IV/IO
 - Reassess in 10 minutes.
 - Repeat dose every 10 minutes as necessary to control severe pain.

- Monitor for respiratory depression
- Promethazine, 25 mg IV/IM/IO every 6 hours as needed for nausea or for synergistic analgesic effect

Note: Narcotic analgesia should be avoided in casualties with respiratory distress, decreased oxygen saturation, shock, or decreased level of consciousness.

Tactical Evacuation (TACEVAC) Care

New #6. Traumatic Brain Injury

a. Casualties with moderate/severe TBI should be monitored for:

- 1) decreases in level of consciousness
- 2) pupillary dilation
- 3) SBP should be >90 mmHg
- 4) O₂ sat > 90
- 5) Hypothermia
- 6) PCO₂ (If capnography is available, maintain between 35-40 mmHg)
- 7) Penetrating head trauma (if present, administer antibiotics)
- 8) Assume a spinal (neck) injury until cleared

b. Unilateral pupillary dilation accompanied by a decreased level of consciousness may signify impending cerebral herniation; if these signs occur, take the following actions to decrease intracranial pressure:

- 1) Administer 250 cc of 3 or 5% hypertonic saline bolus.
- 2) Elevate the casualty's head 30 degrees.
- 3) Hyperventilate the casualty.
 - a) Respiratory rate 20
 - b) Capnography should be used to maintain the end-tidal CO₂ between 30-35
 - c) The highest oxygen concentration (FIO₂) possible should be used for hyperventilation.

Notes:

- Do not hyperventilate unless signs of impending herniation are present.
- Casualties may be hyperventilated with oxygen using the bag-valve-mask technique.

10. Monitoring

Institute pulse oximetry and other electronic monitoring of vital signs, if indicated. All individuals with moderate/severe TBI should be monitored with pulse oximetry. (BTF 2007)

13. Provide analgesia as necessary.

a. Able to fight:

These medications should be carried by the combatant and self-administered as soon as possible after the wound is sustained.

- Mobic, 15 mg PO once a day
- Tylenol, 650-mg bilayer caplet, 2 PO every 8 hours

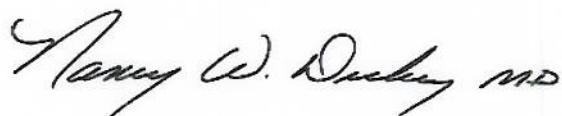
b. Unable to fight:

Note: Have naloxone readily available whenever administering opiates.

- Does not otherwise require IV/IO access
 - Oral transmucosal fentanyl citrate (OTFC), 800 ug transbuccally
 - Recommend taping lozenge-on-a-stick to casualty's finger as an added safety measure
 - Reassess in 15 minutes
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 - Promethazine, 25 mg IV/IM/IO every 6 hours as needed for nausea or for synergistic analgesic effect

Note: Narcotic analgesia should be avoided in casualties with respiratory distress, decreased oxygen saturation, shock, or decreased level of consciousness.

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WORKS CITED

1. Current TBI Numbers, Defense and Veterans Brain Injury Center. Accessed 26 March 2012. <http://www.dvbc.org/TBI-Numbers.aspx>.
2. Gibson D, Helmick K, Jaffee M, et. al. "Traumatic Brain Injury Care in the Department of Defense," Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury, September 2009. Available at: <http://www.dcoe.health.mil/Content/Navigation/Documents/Traumatic%20Brain%20Injury%20Care%20in%20the%20Department%20of%20Defense.pdf>
3. Brain Trauma Foundation Writing Team. Guidelines for Prehospital Management of Traumatic Brain Injury 2nd Edition. *Prehospital Emergency Care* 2007;12(1): S1-S53.
4. Stiver SI, Manley GT. Prehospital Management of Traumatic Brain Injury. *Neurosurg Focus* 2008;25(4):E5
5. Butler FK, Giebner SD, McSwain N, et al., eds. *Prehospital Trauma Life Support Manual: Military Version*. 7th ed. St. Louis: Mosby; 2010.
6. Eastridge BJ, Mabry RL, Blackbourne LH, et. al. We Don't Know What We Don't Know: Prehospital Data in Combat Casualty Care. *The United States Army Medical Department Journal* 2011; Apr-Jun: 11-14.
7. Knuth T, Letarte PB, Ling G, et. al. Guidelines for the Field Management of Combat-Related Head Trauma. Brain Trauma Foundation (Supported by a grant from the Defense and Veterans Brain Injury Center): New York, NY: 2005.
8. Minardi J, Crocco T. Management of Traumatic Brain Injury: First Link in Chain of Survival. *Mt Sinai J Med* 2009;76:138-44.
9. Wolfe TJ, Torbey MT. Management of Intracranial Pressure. *Current Neurology and Neuroscience Reports* 2009;9:477-85.
10. Joint Theater Trauma System Clinical Practice Guideline: Management of Patients with Severe Head Trauma; July 2010.
11. Blackbourne LH, Cole J, Mabry R, et al: The "Silent Killer": Hyperventilation in the Brain Injured. *The United States Army Medical Department Journal* 2008; Jan-Mar:50-55.
12. Strandvik GF: Hypertonic Saline in Critical Care: a Review of the Literature and Guidelines for use in Hypotensive States and Raised Intracranial Pressure. *Anaesthesia* 2009;64:990-1003.

13. Meyer MJ, Megyesi J, Meythaler J, et al. Acute Management of Acquired Brain Injury Part II: an Evidence-Based Review of Pharmacological Interventions. *Brain Injury* 2010;24(5):706-21.
14. Bulger EM, May S, Brasel KJ, et al: Out-of-Hospital Hypertonic Resuscitation Following Severe Traumatic Brain Injury. *JAMA* 2010;304(13):1455-64.
15. Rockswold GL, Solid CA, Paredes-Andrade E, et al: Hypertonic Saline and its Effect on Intracranial Pressure, Cerebral Perfusion Pressure, and Brain Tissue Oxygen. *Neurosurgery* 2009;65(6):1035-42.
16. Benyamin R, Trescot AM, Datta S. Opioid Complications and Side Effects. *Pain Physician* 2008;11:S105-S120.
17. Walters FJM. Neuropharmacology – Intracranial Pressure and Cerebral Blood Flow. *Pharmacology* 1998; 9, article 7. Available at: http://www.nda.ox.ac.uk/wfsa/html/u09/u09_019.htm. Accessed 23 March 2012.
18. Jeremitsky E, Omert L, Dunham M, et al. Harbingers of Poor Outcome the Day After Severe Brain Injury; Hypothermia, Hypoxia, and Hypoperfusion. *J Trauma* 2003;54:312-19.
19. Konstantinidis A, Inaba K, Dubose J, et al: The Impact of Nontherapeutic Hypothermia on Outcomes After Severe Traumatic Brain Injury. *J Trauma* 2011;71(6):1627-31.
20. Meyer M, Megyesi J, Meythaler J: Acute Management of Acquired Brain Injury Part I: an Evidence-Based Review of Non-Pharmacological Interventions. *Brain Injury* 2010;24:694-705.
21. Roberts I, Schierout G. Hyperventilation Therapy for Acute Traumatic Brain Injury. Cochrane Database of Systematic Reviews 1997; Issue 4, Art. No.: CD0005666. (Review assessed as up-to-date 6 Jan 2008).
22. Floyd T, Clark J, Gelfand R, et al. Independent Cerebral Vasoconstrictive Effects of Hyperoxia and Accompanying Arterial Hypocapnia at 1 ATA. *J Appl Physiol* 2003;95:2453-61.
23. Tisdall MM, Taylor C, Tachtisidis I, et al: The Effect of Cerebral Tissue Oxygenation Index of Changes in the Concentrations of Inspired Oxygen and End-Tidal Carbon Dioxide in Healthy Adult Volunteers. *Anesth Analg* 2009;109(3):906-13.
24. Tolias CM, Reinert M, Seiler R, et al. Normobaric Hyperoxia-induced Improvement in Cerebral Metabolism and Reduction in Intracranial Pressure in Patients with Severe Head Injury: a Prospective Historical Cohort-matched Study. *J Neurosurg* 2004;101:435-444.
25. Tolias CM, Kumaria A, Bullock MR: Letter to the Editor: Hyperoxia and Traumatic Brain Injury. *J Neurosurg* 2009;110:607-609.

26. Bergsneider M., Hovda DA., Lee SM., et. al. Dissociation of Cerebral Glucose Metabolism and Level of Consciousness During the Period of Metabolic Depression Following Human Traumatic Brain Injury. *J. Neurotrauma* 2000; 1: 389–401.
27. Bergsneider M., Hovda DA., Shalmon E., et. al. Cerebral Hyperglycolysis Following Severe Traumatic Brain Injury in Humans: a Positron Emission Tomography Study. *J. Neurosurg.* 1997; **86**: 241–251.
28. Hospenthal DR, Murray CK, Andersen RC, et. al. Guidelines for the Prevention of Infections Associated with Combat-Related Injuries: 2011 Update-Endorsed by the Infectious Diseases Society of American and the Surgical Infection Society. *J Trauma* 2011; **71**(2):S210-S234.
29. Antibiotic Prophylaxis for Penetrating Brain Injury. *J Trauma*; **51**:S34-S40.

ADDITIONAL REFERENCES

Brain Trauma Foundation: Guidelines for the Management of Severe Traumatic Brain Injury. 3rd Edition. *J Neurotrauma* 2007. **24**:S1-S106.

Cap AP, Spinella PC: Severity of Head Injury is Associated with Increased Risk of Coagulopathy in Combat Casualties. *J Trauma* 2011; **71**:S78-S81.

Champion HR: Combat Fluid Resuscitation: Introduction and Overview of Conferences. *J Trauma* 2003; **54**(5, suppl):7.

Chi J, Knudson M, Vassar M, et al: Prehospital Hypoxia Affects Outcome in Patients with Traumatic Brain Injury: a Prospective Multicenter Study. *J Trauma* 2006; **61**:1134-1141.

Dubose J, Kobayashi L, Lozornio A, et al. Clinical Experience Using 5% Hypertonic Saline as a Safe Alternative Fluid for Use in Trauma. *J Trauma* 2010; **68**:1172-1177.

Defense and Veterans Brain Injury Center Working Group. Clinical Practice Guidelines for the Management of Mild Traumatic Brain Injury in Military Operations Settings; 2006.

Feldman Z, Kanter M, Robertson C, et al: Effect of Head Evaluation on Intracranial Pressure, Cerebral Perfusion Pressure, and Cerebral Blood Flow in Head-Injured Patients. *J Neurosurg* 1992; **76**:207-11.

Fessler R, Diaz F: The Management of Cerebral Perfusion Pressure and Intracranial Pressure after Severe head injury. *Ann Emerg Med* 1993; **22**:998-1003.

Holcomb J. Fluid Resuscitation in Modern Combat Casualty Care: Lessons Learned in Somalia. *J Trauma* 2003; **54**:S46-51.

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Ivascu F, Howells G, Junn F, et al: Predictors of Mortality in Trauma Patients with Intracranial Hemorrhage on Pre-injury Aspirin or Clopidogrel. *J Trauma* 2008;65:785-788.

Ling G, Rhee P, Ecklund J. Surgical Innovations Arising from the Iraq and Afghanistan Wars. *Annu Rev Med* 2010;61:457-468.

Manley G, Knudson M, Morabito D. Hypotension, Hypoxia, and Head Injury. *Arch Surg* 2001;136:1118-1123

Moraine J, Berré J, Mélot C. Is Cerebral Perfusion Pressure a Major Determinant of Cerebral Blood Flow During Head Elevation in Comatose Patients with Severe Intracranial Lesions? *J Neurosurg* 2000;92:606-614.

Memorandum, Defense Health Board to Assistant Secretary of Defense (Health Affairs), Combat Ready Clamp; 23 Sept 2011.

Memorandum, Defense Health Board to Assistant Secretary of Defense (Health Affairs), Fluid Resuscitation in TCCC, 10 Dec 2010.

Memorandum, Defense Health Board to Assistant Secretary of Defense (Health Affairs), Tranexamic Acid; 23 Sept 2011.

Rickard A: Hypertonic Sodium Solution versus Mannitol in Reducing ICP in Traumatic Brain Injury. *Emerg Med J* 2011;28:75-76.

Salehpour F, Bazzazi A, Porhomayon J, Nader N: Correlation between coagulopathy and outcome in severe head trauma in neurointensive care and trauma units. *J Crit Care* 2011;Epub ahead of print.

Stahel P, Smith W, Moore E: Current trends in resuscitation strategy for the multiply injured patient. *Int J Care Injured* 2009;40(Suppl 4):S27-S35.

Timmons S: Current Trends in Neurotrauma Care. *Crit Care Med* 2010;38:S431-S444.

Torre-Healy A, Marko N, Well R. Hyperosmolar Therapy for Intracranial Hypertension. *Neurocrit Care* 2011;Epub ahead of print.

Wafaisade A, Lefering R, Tjardes T, et al. Acute Coagulopathy in Isolated Blunt Traumatic Brain Injury. *Neurocrit Care* 2010;12:211-19.